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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/622,893	07/17/2003	Chong-Sheng Yuan	466992001300	5005

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EXAMINER

WALICKA, MALGORZATA A

ART UNIT	PAPER NUMBER
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1652

DATE MAILED: 02/23/2006

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary

Application No.

10/622,893

Applicant(s)

YUAN ET AL.

Examiner

Malgorzata A. Walicka

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-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --
Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 05 November 2005.
- 2a) ☒ This action is **FINAL**. 2b) ☐ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 1,14,15,21-25 and 32-61 is/are pending in the application.
- 4a) Of the above claim(s) _____ is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 1,14,15,21-25 and 32-61 is/are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on _____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some * c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
2. ☐ Certified copies of the priority documents have been received in Application No. _____.
3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).
- * See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

- 1) ☐ Notice of References Cited (PTO-892)
- 2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
- 3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08)
Paper No(s)/Mail Date _____.
- 4) ☐ Interview Summary (PTO-413)
Paper No(s)/Mail Date. _____.
- 5) ☐ Notice of Informal Patent Application (PTO-152)
- 6) ☐ Other: _____.

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Amendment, comprising amendments to the claims specification and figures filed Nov. 25, 2005 is acknowledged. Claims 2-13, 16-20, and 62-86 have been canceled. Claims 1, 15, 32, 45 and 54 have been amended. Claims 1, 14-15, 21-25 and 32-61 are pending and under examination.

Detailed Action

2. Objections

Specification

Objections to description of Fig. 1 made in the Office Action of July 22, 2006 (previous action) are withdrawn, because the description has been amended. Other objections are withdrawn, because Applicants arguments are found persuasive.

Figures

Objection to Fig. 3 for lack of lacks description of Y-axis is withdrawn because the relevant correction has been made.

Claims

Objection to claim 32 is withdrawn, because the claim has been amended.

3. Rejections

3.1. 35 USC § 112, second paragraph

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Claims 54, 78 and 85 were rejected under 35 U.S.C. 112, second paragraph in the previous action. Rejection of claims 78 and 85 is moot, because the claims have been canceled.

Rejection of claim 54 is withdrawn, because the claim has been amended.

Amended claim 1 and dependent claims are rejected because the claim is confusing in recitation "comprising a bacterial leader sequence from about 5 to about 30 amino acid residues, wherein the leader sequence comprises the amino acid sequences set forth in SEQ ID NO: 1".

Firstly, there is only one amino acid sequence identified as SEQ ID NO: 1, thus the plural "sequences set forth in SEQ ID NO: 1" is improper. Secondly SEQ ID NO: 1 consists of 12 amino acids, thus a first peptidyl fragment comprising from about 5 amino acid residues cannot comprise SEQ ID NO: 1 which is 12 amino acid long.

Furthermore, amended claims 15 and 23-24, are specifically rejected because the second bacterial leader cannot comprise SEQ ID NO: 4 which is 17 amino acid long, and at the same time comprise SEQ ID NO: 4 that is about 5 amino acid long.

A broad range or limitation together with a narrow range or limitation that falls within the broad range or limitation (in the same claim) is considered indefinite, since the resulting claim does not clearly set forth the metes and bounds of the patent protection desired. See MPEP § 2173.05(c). Note the explanation given by the Board of Patent Appeals and Interferences in *Ex parte Wu*, 10 USPQ2d 2031, 2033 (Bd. Pat. App. & Inter. 1989), as to where broad language is followed by "such as" and then narrow language. The Board stated that this can render a claim indefinite by raising a question or doubt as to whether the feature introduced by such language is (a) merely exemplary of the remainder of the claim, and therefore not required, or (b) a required feature of the claims. Note also, for example, the decisions

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of *Ex parte Steigewald*, 131 USPQ 74 (Bd. App. 1961); *Ex parte Hall*, 83 USPQ 38 (Bd. App. 1948); and *Ex parte Hasche*, 86 USPQ 481 (Bd. App. 1949).

3.2. 35 USC § 112, first paragraph

3.2.1. *Written description*

Claims 1-10, 12, 14-24, 32-42, 45-66, 69-86 were rejected under 35 U.S.C. 112, first paragraph, in the previous action.

Rejection of claims 2-10, 12, 16-20, 62-66 and 69-86 is moot because the claims have been canceled.

Rejection of claims 1, 14-15, 21-24, 32-42, 45-61 is withdrawn because the claims have been amended.

3.2.2. *Scope of enablement*

Claims 1-12, 14-24, 32-42, 45-66, 69-86 were rejected in the previous action for scope of enablement.

Rejection of claims 2-10, 12, 16-20, 62-66 and 69-86 is moot because the claims have been canceled.

Rejection of claims 1, 14-15, 21-24, 32-42, 45-61 is withdrawn because the claims have been amended.

A. Claims 1-2, 6-14, 21-22 and 32 are rejected in the previous action rejected under 35 U.S.C. 103(a) as being unpatentable over Yoshida et al. (Primary structures of fungal fructosyl amino acid oxidases and their application to the measurement of glycated

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proteins, Eur. Biochem. 1996, 242, 499-5050, Takahashi et al. **A** (Molecular Cloning and Expression of Amadoriase Isoenzyme (Fructosyl Amine-oxygen Oxidoreductase EC 1.5.3) from *Aspergillus fumigatus*, J. Biol. Chemistry 1997, 6, 12505-12307) in view of common knowledge in the field of protein expression as exemplified by US Patent 6,194,200 (Expression Systems for Preparation of Polypeptides in Prokaryotic cells, issued Feb. 27, 2001) further referred to as US Patent.

Rejection of claims 2, 5-13 is moot, because the claims have been cancelled.

Rejection of claims 1, 14, 21 and 32 is maintained, for the reasons explained in the previous office action and reiterated herein.

Yoshida et al teaches the use of several amadoriases, among them of *Aspergillus* species, for determination of the level of blood protein glycation in diabetic patients.

Takahashi et al. teach amadoriase from *Aspergillus* sp. that consists of 438 amino acid residues of which amino acids 2-438 are identical to amino acids 1-437 of SEQ ID NO: 3 of the instant application. Takahashi et al emphasize it is the protein consisting of amino acids residues 2-438, i. e. SEQ ID NO: 3 of the instant application, which is routinely purified from *Aspergillus*; see the comment on page 12306, right column, line 4-6 and N-terminal sequence of amadoriase II in Table IV, page 3443 of the reference Takahashi **B** below mentioned in the comment. Thus Takashi teaches the second polypeptide of claim 1.

Takashi et al. do not disclose a chimeric protein, which comprises a bacterial leader sequence comprising SEQ ID NO: 1 and a second sequence which is their

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amadoriase of 438 amino acids comprising SEQ ID NO:3 of the instant application, however, it is a routine practice in the field of protein expression to express proteins as chimeras containing bacterial leader sequences because these sequences promote secretion and stabilize the expressed protein; see US Patent, Introduction.

It would have been obvious to one having ordinary skill in the art at the time of invention to have a protein consisting of amino acid residues 2-438 of Takahashi et al. amadoriase II and add to its N-terminus a bacterial leader as taught by the US Patent.

The motivation for the modification would be an improvement of the enzyme productivity so as to have a large quantity of pure stable enzyme necessary for measurements of glycated proteins in blood serum. This motivation is provided by Yoshida et al. on page 505, the last sentence. The expectation of success is high because of well-developed and routine use of expressed fusion protein in the art. The leader sequences usually do not interfere with the biological activity of the protein of interest, thus the protein of interest may be used as a fusion protein; see the abstract of the US Patent.

Thus, the claimed invention was within the ordinary skill in the art to make and use at the time it was made, and was as a whole *prima facie* obvious.

Response to applicants arguments

In their REMARKS of Nov. 25, 2005, page 18, third paragraph, Applicants argue the combined references do not teach or suggest a chimeric protein comprising a first

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peptidyl comprising SEQ ID NO: 1 and a second peptidyl comprising an amadoriase comprising the amino acid sequence set forth in SEQ ID NO: 3.

Applicants' argument has been fully considered but is found not persuasive. The prior art does not need to teach the chimeric protein as claimed by the amended claims, because this is not 102 rejection. However, the combined references suggest to make the chimeric proteins comprising an amadoriase disclosed by Takashi and any leading leader sequence attached to its terminus for more efficient expression, as taught by the patent. Although the chimeric protein as claimed by the amended claim 1 is structurally novel, it is obvious.

B. Claims 33-37, 39-41, 45, 53, 54, 57, 58, 59-61 are were rejected under 35 U.S.C. 103(a) as being unpatentable over European Patent EP0 821064 A2, published Jan. 28, 1998 (the EU Patent), included in the IDS, and further in view of Takahashi et al. A and US Patent 6,194,200 as used in the above rejection of the chimeric protein of claim 1.

Claims 33-37, 39-41, 45, 53, 54, 57, 58 remain rejected as directed to the use of the protein of claim 1 in a method for assaying a glycosylated protein in a sample. Claims 59-61 are directed to the kit for such method. The reasons are explained above under section 3.3.1, related to the rejection of the product, as well as for the reasons explained in the previous action.

The additional features of the method recited by claims 38, 40, 42, 46-52, 55-56 are well known features of such amadoriase based assays for the art. Therefore the dependent claims 38, 40, 42, 46-52, 55-56 are included in the rejection.

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C. Claims 62-63, 65, 66, 83 and 85 were rejected as being unpatentable over European Patent EP0 821064 A2, published Jan. 28, 1998 (included in the IDS), in view of common knowledge in biochemistry and Takahashi et al. **B** (Isolation, Purification and Characterization of Amadoriase Isoenzymes (Fructosyl Amine-oxygen Oxidoreductase EC1.5.3) from *Aspergillus* sp., J. Biol. Chem., 1007, 272, 3437-3443). This rejection is now moot, because claims 62-63, 65, 66, 83 and 85 have been canceled.

4. Conclusion

All pending claims 1, 14-15, 21-25 and 32-61 are rejected.

THIS ACTION IS MADE FINAL. Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Malgorzata A. Walicka whose telephone number is (571) 272-0944. The examiner can normally be reached on Monday-Friday from 10:00 a.m. to 4:30 p.m.

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If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Ponnathapura Achutamurthy, can be reached on (571) 272-0928. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Malgorzata A. Walicka, Ph.D.

Art Unit 1652

Patent Examiner



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